the entire repertoire of beads in the planar army or panel formed adjacent to the electrode surface for parallel readout. As with heterogeneous panels in general, the arrangement of beads within the array is either random (with respect to chemical identity), and the identity of beads scoring high in the binding assay must be determined subsequently, or it is spatially encoded by invoking the "Layout-Preserving Transfer" method of sample loading described herein.

The former valiant is readily implemented and accommodates array formation either prior to or subsequent to performing the binding assay. For example, binding may be performed in suspension before beads are assembled into the array. As with the aforementioned cDNA selection procedure, the method of the present invention also accommodates the use of beads as capture elements for end-functionalized target DNA, for example, via biotin-streptavidin complexation. In this later case, beads serve as a delivery vehicle to collect all probe-target complexes to the electrode surface where they are assembled into an array for ease of analysis. In particular, proximity CCD detection of beads on electrodes will benefit from the lensing action of the beads in the array. This version of the assay is preferably used if only a small number of positive scores are expected.

Hybridization to a pre-formed bead array can take advantage of a variant of the assay which preserves spatial encoding. An array of bead clusters is formed by the "Layout-Preserving Transfer" method previously described herein, and exposed to a mixture of cDNAs. The resulting spatial distribution of fluorescence intensity or radioactivity reflects the relative abundance of cDNAs in the mixture. This procedure relies on the detection of a characteristic fluorescence or other signal from the probe-target complex on the surface of a single bead. Given the fact that the array is readily held stationary by the methods of the present invention, image acquisition may be extended to attain robust signal-to-noise for detection of low level signals. For example, a signal generated by a bead of 10 micron diameter with at most 10^8 probe-target complexes on the surface of the bead may be detected. Bead lensing action also aids in detection.

As with the implementation of drug screening, the functional elements of the present invention may be combined to perform multiple preparative and analytical procedures on DNA.

EXAMPLE X

Alignment and Stretching of DNA in Electric Field-Induced Flow

The present invention can be used to position high-molecular weight DNA in its coiled configuration by invoking the fundamental operations as they apply to other colloidal particles. However, in addition, the electrokinetic flow induced by an electric field at a patterned electrode surface may be employed to stretch out the DNA into a linear configuration in the direction of the flow.

Procedures have been recently introduced which rely on optical imaging to construct a map of cleavage sites for restriction enzymes along the contour of an elongated DNA molecule. This is generally known as a "restriction map". These procedures, which facilitate the study of the interaction of these and other proteins with DNA and may also lead to the development of techniques of DNA sequencing, depend on the ability to stretch and align DNA on a planar substrate.

For individual DNA molecules, this has been previously achieved by subjecting the molecule to elongational forces such as those exerted by fluid flow, magnetic fields acting on DNA-anchored magnetic beads or capillary forces. For example, DNA "combs" have been produced by simply placing DNA molecules into an evaporating droplet of electrolyte. If provisions are made to promote the chemical attachment of one end of the molecule to the surface, the DNA chain is stretched out as the receding line of contact between the shrinking droplet and the surface passes over the tethered molecules. This leaves behind dry DNA molecules that are attached in random positions within the substrate area initially covered by the droplet, stretched out to varying degrees and generally aligned in a pattern of radial symmetry reflecting the droplet shape. Linear "brushes", composed of a set of DNA molecules chemically tethered by one end to a common line of anchoring points, have also been previously made by aligning and stretching DNA molecules by dielectrophoresis in AC electric fields applied between two metal electrodes previously evaporated onto the substrate.

The present invention invokes electrokinetic flow adjacent to an electrode patterned by UV-mediated regrowth of oxide to provide a novel approach to the placement of DNA molecules in a predetermined arrangement on a planar electrode surface, and to the stretching of the molecules from their native coil configuration into a stretched, linear configuration that is aligned in a predetermined direction. This process is shown in FIG. 11 and is accomplished by creating controlled gradients in the flow vicinity across the dimension of the DNA coil. The velocity gradient causes different portions of the coil to move at different velocities thereby stretching out the coil. By maintaining a stagnation point at zero velocity, the stretched coil will be fixed in position. This method has several advantages over the prior art approaches. First, DNA molecules in their coiled state are subjected to light control to form arrays of desired shape in any position on the surface. This is possible because large DNA from cosmids or YACs forms coils with a radius in the range of one micron, and thus acts in a manner analogous to colloidal beads. A set of DNA molecules may thus be steered into a desired initial arrangement. Second, UV-patterning ensures that the elongational force created by the electrokinetic flow is directed in a predetermined direction. The presence of metal electrodes in contact with the sample, a disadvantage of the dielectrophoretic prior art method, is avoided by eliminating this source of contamination that is difficult to control especially in the presence of an electric field. On patterned Si/SiOx electrodes, flow velocities in the range of several microns/second have been generated, as required for the elongation of single DNA molecules in flow. Thus, gradients in the flow field determines both the fractional elongation and the orientation of the emerging linear configuration. Third, the present invention facilitates direct, real-time control of the velocity of the electric field-induced flow, and this in turn conveys explicit control over the fractional elongation.

While the invention has been particularly shown and described with reference to a preferred embodiment thereof, it will be understood by those skilled in the art that various changes in form and details may be made therein without departing from the spirit and scope of the invention.

What is claimed is:

1. A method for controlling the movement of particles suspended at an interface between an electrode and an electrolyte solution, the method comprising the following steps:

generating an electric field at said interface between said electrode and said electrolyte solution; and

illuminating the surface of said electrode with a predetermined light pattern to control the movement of said

particles in accordance with said predetermined light pattern and electrochemical properties of said electrode.

2. The method of claim 1, wherein said electric field is at least one of a constant and a time varying electric field.

3. The method of claim 1, further comprising a patterning step which is performed using at least one of UV-mediated oxide regrowth, surface chemical patterning and surface charge profiling.

4. The method of claim 3, wherein said patterning step is used to create a plurality of areas of low impedance on said electrode, and said illuminating step is used to selectively connect one or more of said areas of low impedance to cause said particles to move therebetween in accordance with said patterning and said predetermined light pattern.

5. The method of claim 1, wherein the illuminating step comprises the further step of:

illuminating a selected area of said electrode which in conjunction with a frequency of said electric field causes the particles to move into said selected area.

6. The method of claim 5, wherein the frequency of said electric field is adjusted in order to move said particles out of said selected area.

7. The method of claim 1, wherein the illuminating step comprises the further step of:

illuminating a selected area of said electrode surface with a high intensity light pattern so as to cause the particles to move out of said selected area.

8. The method of claim 1 further comprising a patterning step which creates at least two areas of low impedance on said electrode, and said illuminating step being used to selectively cause said particles to move from a first low impedance area to a second low impedance area.

9. An apparatus for implementing the differential lateral displacement of particles suspended at an interface between an electrode and an electrolyte solution, said apparatus comprising:

an electric field generator which generates an electric field at said interface;

an electrode;

an electrolyte solution having a substantially continuous flow which effects the displacement of said particles in a direction substantially parallel to said interface;

an illumination source which illuminates said electrode with an adjustable, predetermined light pattern; and

a plurality of particles located in said electrolyte solution, said particles being in said electrolyte flow and being displaced by said electric field in conjunction with said predetermined light pattern, said particles being displaced in accordance with variations in physical and chemical properties of said particles which determine the mobility of said particles.

10. The apparatus of claim 9, wherein said electrode is a light sensitive electrode.

11. The apparatus of claim 9, wherein said impedance profile is created by a predetermined illumination pattern.

12. The apparatus of claim 9, wherein:

said electrode patterning includes an area of low impedance bordered by an area of high impedance, said low impedance area including a narrow conduit in communication with a wide conduit, both said conduits being oriented parallel to the direction of said continuous flow of said electrolyte;

said wide conduit including a row of intermittently spaced areas of high impedance barriers traversing the width of said wide conduit;

a portion of said plurality of particles being optically distinguishable from the remaining particles;

a detector for visually inspecting said particles traversing the length of said narrow conduit in response to said continuous flow of electrolyte;

said illumination pattern being substantially in the shape of a rectangle having a longer dimension adjusted to be substantially equal to the width of said wide conduit, said rectangle having a smaller dimension which is adjusted to be substantially equivalent to the diameter of said particles, said pattern being located in front of said barriers, and said illumination pattern conforming to an intensity profile placing a maximal value of intensity in the center of said wide conduit and decreasing symmetrically to lower values of intensity at the two sides of said wide conduit; and

a delay activation circuit which activates said illumination profile in response to a signal derived from said visual inspection of said particles so as to cause an illuminated particle to be displaced from regions of maximum intensity to regions of lower intensity of said intensity profile and to be deflected into the intermittent spaces between said barriers.

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point at zero velocity, the shed coil will be fixed in position This method has several advantages over the prior art approaches. First, DNA molecules in their coiled state are subjected to light control to form arrays of desired shape in any position on the surface. This is possible because large DNA from cosmids or YACs forms coils with a radius in the range of one micron, and thus acts in a manner analogous to colloidal beads. A set of DNA molecules may thus be steered into a desired initial arrangement. Second, UV-patterning ensures that the elongational force created by the electrokinetic flow is directed in a predetermined direction. The presence of metal electrodes in contact with the sample, a disadvantage of the dielectrophoretic prior art method, is avoided by eliminating this source of contamination that is difficult to control especially in the presence of an electric field. On patterned Si/SiOx electrodes, flow velocities in the range of several microns/second have been generated, as required for the elongation of single DNA molecules in flow. Thus, gradients in the flow field determines both the fractional elongation and the orientation of the emerging linear configuration. Third, the present invention facilitates direct, real-time control of the velocity of the electric field-induced flow, and this in turn conveys explicit control over the fractional elongation.

While the invention has been particularly shown and described with reference to a preferred embodiment thereof, it will be understood by those skilled in the art that various changes in form and details may be made therein without departing from the spirit and scope of the invention.

What is claimed is:

1. A method for moving particles suspended at an interface between an electrode and electrolyte solution comprising the following steps:

providing a first electrode positioned in a first plane, and a second electrode positioned in a second plane different from the first plane, an electrolyte solution located therebetween and a plurality of particles suspended in the electrolyte solution, wherein the second electrode comprises a planar electrode having a surface and an interior, the surface or interior having been modified to produce spatial modulations in electrochemical properties of the second electrode; and

generating an electric field at an interface between the electrolyte solution and the second electrode to effect movement of the particles, wherein the movement of the particles at the interface is in accordance with the electric field in combination with the spatial modulations in the properties of the second electrode, said properties affecting the local distribution of the electric field at the interface.

2. The method of claim **1**, wherein said patterning step is used to create one or more areas of low impedance on said electrode.

3. The method of claim **2**, wherein at least one of the frequency or magnitude of the applied voltage is adjusted so as to cause said particles to move preferentially into or out of one or more of said areas of low impedance.

4. The method of claim **1**, wherein said electrode includes a silicon electrode which is coated with a dielectric layer.

5. The method of claim **1**, wherein the spatial modulations of the properties of the second electrode are produced by patterning the surface or the interior of the second electrode by spatially modulated oxide growth, surface chemical patterning or surface profiling.

6. The method of claim **1**, wherein the first electrode and the second electrode each comprises a planar electrode, said first and second electrodes being parallel to another and separated by a gap, with the electrolyte solution containing the particles being located in the gap.

7. The method of claim **1**, wherein the property of the second electrode being modulated comprises impedance, one or more areas of the surface or the interior of the second electrode being modified to exhibit low impedance, and wherein the particles move to the areas of low impedance.

8. The method of claim **1**, wherein the electric field is generated by applying an AC voltage between the first and the second electrode.

9. The method of claim **1**, wherein the second electrode comprises a light-sensitive electrode, the method further comprising the step of illuminating the second electrode with a predetermined light pattern.

10. The method of claim **1**, wherein the movement of the particles is in a direction substantially parallel to the second electrode.

11. A method for controlling the movement of an electrolyte solution comprising the following steps:

providing a first electrode positioned in a first plane, and a second electrode positioned in a second plane different from the first plane, and an electrolyte solution located therebetween, wherein the second electrode comprises a planar electrode having a surface and an interior, the surface or interior having been modified to produce spatial modulations in electrochemical properties of the second electrode; and

generating an electric field at an interface between the electrolyte solution and the second electrode to create fluid flow of the electrolyte solution having a velocity, said velocity having a magnitude determined by said electric field and a direction determined by said spatial modulations in the properties of the second electrode, said properties affecting the local distribution of the electric field at the interface.

12. The method of claim **11**, wherein the spatial modulations of the properties of the second electrode are produced by patterning the surface or the interior of the second electrode by spatially modulated oxide growth, surface chemical patterning or surface profiling.

13. The method of claim **11**, wherein the property of the second electrode being modulated comprises impedance, one or more areas of the surface or the interior of the second electrode being modified to exhibit low impedance, and wherein the electrolyte solution moves to the areas of low impedance.

14. The method of claim **11**, wherein the first electrode and the second electrode each comprises a planar electrode, said first and second electrodes being parallel to another and separated by a gap, with the electrolyte solution being located in the gap.

15. The method of claim **11**, wherein the electric field is generated by applying an AC voltage between the first and the second electrode.

16. The method of claim **11**, wherein the second electrode comprises a light-sensitive electrode, the method further comprising the step of illuminating the second electrode with a predetermined light pattern.

17. The method of claim **11**, wherein the second electrode comprises a silicon electrode.

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art approaches. First, DNA molecules in their coiled state are subjected to light control to form arrays of desired shape in any position on the so. This is possible because large DNA from cosmids or YACs forms coils with a radius in the range of one micron, and thus acts in a manner analogous to colloidal beads. A set of DNA molecules may thus be steered into a desired initial arrangement. Second, UV-patterning ensures that the elongational force created by the electrokinetic flow is directed in a predetermined direction. The presence of metal electrodes in contact with the sample, a disadvantage of the dielectrophoretic prior art method, is avoided by eliminating this source of contamination that is difficult to control especially in the presence of an electric field. On patterned Si/SiOx electrodes, flow velocities in the range of several microns/second have been generated, as required for the elongation of single DNA molecules in flow. Thus, gradients in the flow field determines both the fractional elongation and the orientation of the emerging linear configuration. Third, the present invention facilitates direct, real-time control of the velocity of the electric field-induced flow, and this in turn conveys explicit control over the fractional elongation.

While the invention has been particularly shown and described with reference to a preferred embodiment thereof, it will be understood by those skilled in the art that various changes in form and details may be made therein without departing from the spirit and scope of the invention.

What is claimed is:

1. A method of dynamically assembling an array of particles at an interface between an electrode and an electrolyte solution, the method comprising the following steps:

providing an electrode, an electrolyte solution and an interface therebetween;

providing a plurality of particles located in said electrolyte solution;

illuminating said electrode with a predetermined light pattern; and

generating an electric field at said interface to cause the assembly of an array of particles in accordance with the predetermined light pattern of said electrode.

2. The method of claim 1, further comprising the step of maintaining said particles in accordance with said assembly by either maintaining said electric field and said predetermined light pattern, chemically linking said particles, or confining said particles.

3. The method of claim 1, further comprising the step of removing said electric field to thereby cause the disassembly of said array of particles.

4. The method of claim 1, wherein said predetermined light pattern is adjusted to reconfigure said particle array in accordance with said predetermined light pattern.

5. An array of particles formed by the method of dynamically assembling the array of particles at an interface between an electrode and an electrolyte solution, the method comprising the following steps:

providing an electrode, an electrolyte solution and an interface therebetween;

providing a plurality of particles located in said electrolyte solution;

illuminating said electrode with a predetermined light pattern; and

generating an electric field at said interface to cause the assembly of an array of particles in accordance with the predetermined light pattern of said electrode.

6. The array of claim 5, wherein said particle array is compositionally random and said particles are chemically encoded to include chemically or physically distinguishable characteristics.

7. An apparatus for assembling an array of particles comprising

an electrode, an electrolyte solution and an interface therebetween; and

a plurality of particles suspended in said electrolyte solution, wherein the apparatus is configured such that, when an electric field is generated at the interface and the electrode is illuminated with a pre-determined light pattern, the illumination in combination with the generation of an interfacial electric field results in a formation of a planar array of particles in a designated area of the electrode, said designated area being defined by the pattern of illumination.

8. The apparatus of claim 7, wherein the electrode comprises a light-sensitive electrode.

9. The apparatus of claim 8, further comprising an additional electrode, wherein the light-sensitive electrode and the additional electrode each comprise a planar electrode, the electrodes being parallel to one another and separated by a gap, the plurality of particles and the electrolyte solution being located in said gap.

10. The apparatus of claim 9, wherein the interfacial electric field is generated by applying an AC voltage between the additional and the light-sensitive electrode.

11. The apparatus of claim 9, wherein the additional electrode comprises an optically transparent electrode that allows detection of the particles in the array by means of optical microscopy in conjunction with a recording device.

12. The apparatus of claim 11, wherein the recording device comprises a charge-coupled device (CCD).

13. The apparatus of claim 9, wherein the light-sensitive electrode and the additional electrode are contained in an electrochemical cell that is fluidically connected to the exterior of said cell to allow fluid entry and exit into and out of the cell.

14. The apparatus of claim 7, wherein the electrode comprises a silicon electrode.

15. The apparatus of claim 7, wherein the designated area corresponds to an area of low interfacial impedance.

16. The apparatus of claim 7, wherein the electrode has been modified to produce spatial modulations in electrochemical properties of the electrode that affect the local distribution of the interfacial electric field, such that when the electric field is generated at the interface, the designated area of the particle array formation is defined by the pattern of illumination in combination with the spatial modulation in the electrode properties.

17. The apparatus of claim 16, wherein the spatial modulations in the properties of the electrode are provided by patterning the electrode by spatially modulated oxide growth, surface chemical patterning or surface profiling.

18. The apparatus of claim 7, further comprising a light-source for illuminating the electrode and an electric field generator for generating the interfacial electric field.

19. The apparatus of claim 7, wherein the particles are arranged in a planar array.

20. The apparatus of claim 19, wherein the array is immobilized by chemical or physical means.

21. The apparatus of claim 19, wherein the particles comprise beads having biomolecules attached thereto, wherein the beads comprise different bead types distinguish

able by said biomolecules and further distinguishable by a unique chemical or physical characteristic that identifies each bead type.

22. The apparatus of claim **21**, wherein the beads of each type are encoded with a chemical label that uniquely identifies said bead type.

23. The apparatus of claim **21**, wherein the biomolecules are selected from the group consisting of peptides, proteins, oligonucleotides, nucleic acids, ligands, receptors, antibodies and antigens.

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